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Applicant:	Jeffrey R. Stinson et al.	Art Unit:	1645
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Title:	HUMANIZED MONOCLONAL ANTIBODIES THAT PROTECT AGAINST SHIGA TOXIN INDUCED DISEASE		

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
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DECLARATION OF DR. HING WONG

I declare:

1. I am an inventor of the subject matter that is described and claimed in the above-captioned patent application.

2. The experiments described in the Edwards et al. ((V110/11:113 page 113 (1997)) publication that relate to the invention were the joint contribution of the instant inventors alone, notwithstanding the inclusion of additional authors on the publication. The other named authors, Ana Edwards and Kathy Arbuthnott, acted on matters concerning the invention under the direction and supervision of the named inventors, and did not contribute to the conception of the presently claimed invention.

3. All statements made herein of my own knowledge are true and all statements made on information and belief are believed to be true; and further these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patents issued thereon.

May 24, 2007
Date

Dr. Hing Wong

V110/VII

HUMANIZATION OF MONOCLONAL ANTIBODIES AGAINST *ESCHERICHIA COLI* TOXINS STX1 AND STX2

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The murine monoclonal antibodies 13C4 and 11E10 are specific for the Shiga toxins types 1 and 2, respectively, that are expressed by Enterohemorrhagic *E. coli*. These antibodies are capable of neutralizing the toxins both in tissue culture and animal models. For the purpose of developing therapeutic agents to treat or prevent hemolytic uremic syndrome, we have humanized these monoclonals. Total RNA from the hybridoma cell lines and mouse antibody variable region primer sets were used for RT-PCR to amplify the variable regions. The V regions were then cloned into a mammalian expression vector for the production of mouse variable region:human IgG1/kappa chimeric antibodies. NS0 cells were transfected with the vector and the humanized antibodies produced recognize the toxins in an enzyme immunoassay. The protective capacity of these antibodies in an animal model system is being tested and the results will be discussed.

V111/VII

THE RESISTIVE INDEX IN D+ AND D- HUS: IS THERE A CLINICAL CORRELATION?

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Several reports have documented the utility of the resistive index (RI) obtained with Doppler sonography in the acute phase of HUS as clinically significant and a potential guide to therapy. We analyzed our experience with RI in children with both D+ and D- HUS with a view toward predicting the need for therapy and prognosis. Sixteen children with HUS had renal Doppler ultrasonography early in the course of their illness. Eleven children, mean age 7.0 y had D+ HUS, the remaining 5, mean age 0.9 y had D- HUS [Denys-Drash (2), meningococcemia, *S. pneumoniae* and idiopathic]. RIs were determined blindly without knowledge of the type of HUS and read as normal or elevated for age. Abnormal RIs were observed in 6/11 children with D+ HUS. Anuria was present in only 3/6 cases, all have normal renal function on follow-up. Of the 5 with normal RIs, 3 had anuria, 1 has decreased renal function. All 5 patients with D- HUS had normal RIs: 4 required dialysis, 2 have normal renal function. We conclude that the RI offers no value in determining the need for dialysis and should not be performed routinely. Patients with D- HUS who would be expected to have increased renovascular resistance by the nature of their pathology did not demonstrate this abnormality on Doppler sonography.